

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant	: Wettstein et al.	Art Unit	: 1644
Serial No.	: 10/587,925	Examiner	: Marianne Dibrino
Filed	: December 4, 2006	Conf. No.	: 1016
Title	: COMPLEXED POLYPEPTIDE AND ADJUVANT FOR IMPROVED VACCINES		

Mail Stop Amendment

Commissioner for Patents

P.O. Box 1450

Alexandria, VA 22313-1450

DECLARATION OF NANCY D. BORSON UNDER 37 C.F.R. § 1.131

I, Nancy D. Borson, hereby declare as follows:

1. I am an inventor of the currently pending claims of the above-referenced patent application.

2. In an Office Action dated January 6, 2010, claims 1-3, 6, 8, 9, 16, 20, and 24 were rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over the Schirmbeck *et al.* reference (*J. Immunol.*, 171:5198-5207 (2003)) in view of the Vives *et al.* reference (*J. Biol. Chem.*, 272(25):1610-1617 (1997)).

3. A printout from PubMed (Exhibit 1) shows the publication date of the Schirmbeck *et al.* reference as being November 15, 2003.

4. Prior to November 15, 2003, and thus necessarily before the publication date of the Schirmbeck *et al.* reference, I worked together with Michael A. Strausbauch, Peter J. Wettstein, and Heather A. Hardin in this country to conceive and reduce to practice the invention recited in claims 1-3, 6, 16, 20, and 24 of the above-referenced application, as evidenced by a copy of Michael A. Strausbauch's laboratory notebook pages. The copy of Michael A. Strausbauch's laboratory notebook pages is attached as Exhibit 2. The date, which is earlier than November 15, 2003, was blocked out.

5. I hereby declare that all statements made herein of my knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patents issued thereon.

04.07.2010
Date

Nancy D. Borson
Nancy D. Borson

Display Settings: Abstract

J Immunol. 2003 Nov 15;171(10):5198-207.

Antigenic epitopes fused to cationic peptide bound to oligonucleotides facilitate Toll-like receptor 9-dependent, but CD4+ T cell help-independent, priming of CD8+ T cells.

Schirmbeck R, Riedl P, Zurbriggen R, Akira S, Reimann J.

Department of Medical Microbiology and Immunology, University of Ulm, Ulm, Germany. reinhold.schirmbeck@medizin.uni-ulm.de

A priority in current vaccine research is the development of adjuvants that support the efficient priming of long-lasting, CD4(+) T cell help-independent CD8(+) T cell immunity. Oligodeoxynucleotides (ODN) with immune-stimulating sequences (ISS) containing CpG motifs facilitate the priming of MHC class I-restricted CD8(+) T cell responses to proteins or peptides. We show that the adjuvant effect of ISS(+) ODN on CD8(+) T cell priming to large, recombinant Ag is enhanced by binding them to short, cationic (arginine-rich) peptides that themselves have no adjuvant activity in CD8(+) T cell priming. Fusing antigenic epitopes to cationic (8- to 10-mer) peptides bound to immune-stimulating ISS(+) ODN or nonstimulating NSS(+) ODN (without CpG-containing sequences) generated immunogens that efficiently primed long-lasting, specific CD8(+) T cell immunity of high magnitude. Different MHC class I-binding epitopes fused to short cationic peptides of different origins showed this adjuvant activity. Quantitative ODN binding to cationic peptides strikingly reduced the toxicity of the latter, suggesting that it improves the safety profile of the adjuvant. CD8(+) T cell priming supported by this adjuvant was Toll-like receptor 9 dependent, but required no CD4(+) T cell help. ODN (with or without CpG-containing sequences) are thus potent Th1-promoting adjuvants when bound to cationic peptides covalently linked to antigenic epitopes, a mode of Ag delivery prevailing in many viral nucleocapsids.

PMID: 14607920 [PubMed - indexed for MEDLINE]

Publication Types, MeSH Terms, Substances

LinkOut - more resources

Next experiment for patent stuff -

gel shift assay.

1. Purposes: show - complexed and free - CpG oligo mixed w peptides on polygel and stain all components

2. Hypo. - CpG thiophosphate will form disulfide bonds w/ cys containing peptides.

∴ complexed & Non complexed CpG + peptide will migrate differently in native poly gel (Reduced & Oxidized forms).

3. Materials - poly gel.

- glycerol for loading buffer

1 - KCSRNR-Hy1 x2 = 10 total.

2 KCSRNR Hy1 6 + CpG

3 AASANA Hy1 7 + ~~AASANA-Hy1~~

4 ACSANA Hy1 = 13 wells

5 ~~Hy1~~

complexed

14 wells.

Gel is 15% TrisHCl 10well

Guthione 1mg/ml ?? right conc?

method.

	KCSAUR	KCSAUR	KCSAUA	KCSANA	5 removed	CP	HYI	CPG	HYI
Result	or	or	or	or		or	or	need	need
	11	22	33	44		66	77	6	7
			← Peaker			← little flatter			
all violet unless noted.			↑ more Blue but just a hint.			Blue	↑ more Violet	↑ faint Blue	